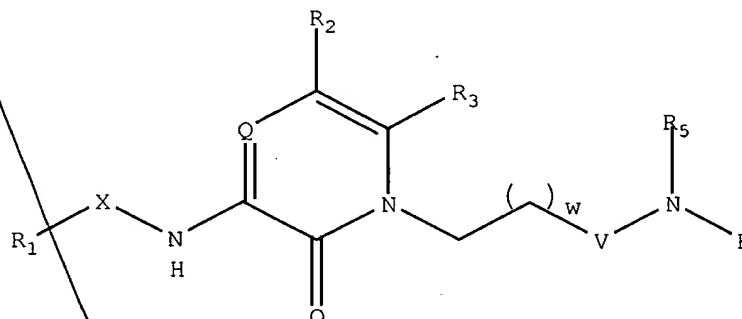


We claim:

1. A compound of the formula:



(a) X is selected from the group consisting of
-S(O)₂-, -N(R')-S(O)₂-, -S(O)₂-N(R')-, -C(=O)-, -OC(=O)-,
-NHC(=O)-, -C(=O)N(R')-, -P(O)(R')- and a direct link, wherein R'
15 is independently hydrogen, alkyl of 1 to about 4 carbon atoms,
aryl of about 6 to about 14 carbon atoms, aralkyl of about 7 to
about 16 carbon atoms, with the proviso that when X is -P(O)(R')-
, the R' is not hydrogen;

(b) R₁ is selected from the group consisting of:

(1) alkyl of 1 to about 12 carbon atoms which is
optionally substituted with Y₁ and/or Y₂,

(2) alkyl of 1 to about 6 carbon atoms
substituted with cycloalkyl of about 3 to about 8 carbon atoms
which is optionally mono-, di-, or tri-substituted with Y₁, Y₂
25 and/or Y₃,

(3) cycloalkyl of 3 to about 15 carbon atoms,
which is optionally mono-, di-, or tri-substituted on the ring
with Y₁, Y₂ and/or Y₃,

(4) heterocycloalkyl of 4 to about 10 ring atoms
30 with the ring atoms selected from carbon and heteroatoms, wherein
the heteroatoms are selected from the group consisting of oxygen,

nitrogen, and $S(O)_i$, wherein i is 0, 1 or 2, which is optionally mono-, di-, or tri-substituted on the ring with Y_1 , Y_2 and/or Y_3 ,

(5) heterocyclo of 4 to about 10 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from the group consisting of oxygen,

nitrogen, and $S(O)_i$, including $\text{---}\text{N}\text{---}\text{G}$, wherein $\text{---}\text{N}\text{---}\text{G}$ is a 5 to 7 member heterocycle of 3 to 6 ring carbon atoms, where G is $\text{---CH}_2\text{---}$, ---O--- , ---S(=O)--- , $\text{---S(O)}_2\text{---}$ or ---S--- , which is optionally mono-, di-, or tri-substituted on the ring carbons with Y_1 , Y_2 and/or Y_3 ,

(6) alkenyl of 2 to about 6 carbon atoms which is optionally substituted with cycloalkyl of 3 to about 8 carbon atoms, which is optionally mono-, di-, or tri-substituted on the ring carbons with Y_1 , Y_2 and/or Y_3 ,

(7) aryl of about 6 to about 14 carbon atoms which is optionally mono-, di- or tri-substituted with Y_1 , Y_2 , and/or Y_3 ,

(8) heteroaryl of about 5 to about 14 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from oxygen, nitrogen, and sulfur, and which is optionally mono-, di-, or tri-substituted with Y_1 , Y_2 , and/or Y_3 ,

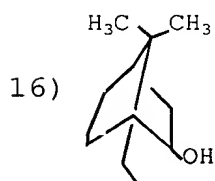
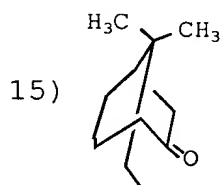
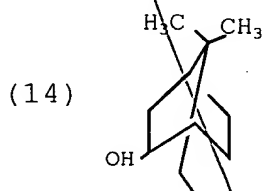
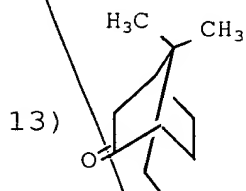
(9) aralkyl of about 7 to about 15 carbon atoms which is optionally substituted on the alkyl chain with hydroxy or halogen and which is optionally mono-, di-, or tri-substituted in the aryl ring with Y_1 , Y_2 , and/or Y_3 ,

(10) heteroaralkyl of 5 to 14 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from oxygen, nitrogen, and sulfur, and which is optionally substituted on the alkyl chain with hydroxy

or halogen and which is optionally mono-, di- or tri-substituted on the ring with Y_1 , Y_2 , and/or Y_3 ,

(11) aralkenyl of about 8 to about 16 carbon atoms which is optionally mono-, di-, or tri-substituted on the aryl ring with Y_1 , Y_2 , and/or Y_3 ,

(12) heteroaralkenyl of 5 to 14 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from oxygen, nitrogen, and sulfur, and which is optionally mono-, di- or tri-substituted on the ring with Y_1 , Y_2 , and/or Y_3 ,



5 (17) fused carbocyclic alkyl of about 5 to about 15 carbon atoms,

(18) difluoromethyl or perfluoroalkyl of 1 to about 12 carbon atoms,

(19) perfluoroaryl of about 6 to about 14 carbon atoms,

10 (20) perfluoroalkyl of about 7 to about 15 carbon atoms, and

(21) hydrogen when X is a direct link;

wherein

5 (i) each Y_1 , Y_2 , and Y_3 is independently selected from the group consisting of halogen, cyano, nitro, tetrazolyl optionally substituted with alkyl of 1 to about 6 carbon atoms, guanidino, amidino, methylamino, methylguanidino, - CF_3 , - CF_2CF_3 , - $CH(CF_3)_2$, - $C(OH)(CF_3)_2$, - OCF_3 , - OCF_2CF_3 , - OCF_2H , - $OC(O)NH_2$, - $OC(O)NHZ_1$, - $OC(O)NZ_1Z_2$, - $NHC(O)Z_1$, - $NHC(O)NH_2$, - $NHC(O)NHZ_1$, - $NHC(O)NZ_1Z_2$, - $C(O)OH$, - $C(O)OZ_1$, - $C(O)NH_2$, - $C(O)NHZ_1$, - $C(O)NZ_1Z_2$, - $P(O)_3H_2$, - $P(O)_3(Z_1)_2$, - $S(O)_3H$, - $S(O)_pZ_1$, - Z_1 , - OZ_1 , - OH , - NH_2 , - NHZ_1 , - NZ_1Z_2 , N-morpholino, and - $S(O)_p(CF_2)_qCF_3$, wherein p is 0, 1 or 2, q is an integer from 0 to 5, and Z_1 and Z_2 are independently selected from the group consisting of alkyl of 1 to 25 about 12 carbon atoms, aryl of about 6 to about 14 carbon atoms, heteroaryl of about 5 to about 14 atoms having 1 to about 9 carbon atoms, aralkyl of about 7 to about 15 carbon atoms, and heteroaralkyl of about 5 to about 14 ring atoms, or

30 (ii) Y_1 and Y_2 are selected together to be - $O[C(Z_3)(Z_4)]_rO-$ or - $O[C(Z_3)(Z_4)]_{r+1}-$, wherein r is an integer from 1 to 4 and Z_3 and Z_4 are independently selected from the group consisting of hydrogen, alkyl or 1 to about 12 carbon atoms, aryl

of about 6 to about 14 carbon atoms, heteroaryl of about 5 to about 14 ring atoms having 1 to about 9 carbon atoms, aralkyl of about 7 to about 15 carbon atoms, and heteroaralkyl of about 5 to about 14 ring atoms;

(c) Q is -N- or -C(R₄)-;

(d) R₂ is selected from the group consisting of hydrogen, halogen and alkyl of 1 to about 6 carbon atoms;

(e) R₃ is selected from the group consisting of hydrogen, alkyl 1 to about 6 carbon atoms, cycloalkyl of 3 to about 7 carbon atoms, alkoxy of 1 to about 6 carbon atoms, halogen, and trifluoromethyl;

(f) alternatively, R₂ and R₃ are selected together and are -(CH₂)_k- where k is 3 or 4;

(g) R₄ is selected from the group consisting of hydrogen, alkyl of 1 to about 8 carbon atoms, hydroxy, alkoxy of 1 to about 8 carbon atoms, aralkyl of 7 to about 15 carbon atoms, alkyl of 1 to about 5 carbon atoms substituted with cycloalkyl of 3 to about 8 carbon atoms, -NHR₈, -S(O)_tR₈ and -C(=O)R₈ where t is 0, 1 or 2;

(h) w is 0, 1 or 2;

(i) V is -CH(R₉)-, -C(=O)-, -O-, -S(O)₂- or a direct link;

(j) R₅ is hydrogen or alkyl of 1 to about 6 carbon atoms;

(k) E is heteroaryl of about 6 to about 10 ring atoms having from 1 to about 4 ring nitrogen atoms and the remainder of the ring atoms carbon atoms and which is substituted with R₆ and R₇;

(l) R₆ and R₇ are independently selected from the group consisting of hydrogen, halogen, hydroxy, alkyl of 1 to about 6

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carbon atoms, alkoxy of 1 to about 6 carbon atoms, alkyl of 1 to about 4 carbon atoms substituted with alkoxy of 1 to about 4 carbon atoms, trifluoromethyl, $-C(=O)OR_{10}$, $-NHR_{10}$, $-C(=O)R_{10}$, $-C(=O)NHR_{10}$, $-OC(=O)NHR_{10}$, $-C(=NR_{10})NHR_{11}$, and $-N(R_{12})-C(=NR_{10})NHR_{11}$; and

(m) R_8 , R_9 , R_{10} , R_{11} and R_{12} are independently selected from the group consisting of hydrogen, alkyl of 1 to about 6 carbon atoms and $-(CF_2)_jCF_3$ wherein j is 0, 1, 2 or 3; and pharmaceutically acceptable salts thereof.

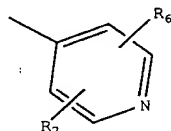
2. A compound according to claim 1 wherein V is $-CH(R_9)-$.

3. A compound according to claim 2 wherein R_9 is hydrogen.

4. A compound according to claim 3 wherein X is $-S(O)_2-$ or a direct link.

5. A compound according to claim 4 wherein R_1 is substituted or unsubstituted aralkyl.

6. A compound according to claim 5 wherein E is



7. A compound according to claim 6 wherein R_6 and R_7 are independently hydrogen or halogen.

8. A compound according to claim 7 wherein at least one of R_6 and R_7 is hydrogen.

9. A compound according to claim 8 wherein Q is $-C(R_4)-$.

10. A compound according to claim 9 wherein w is 1.

11. A compound according to claim 8 wherein Q is -N-.

12. a compound according to claim 11 wherein w is 1.

13. A compound according to claim 2 wherein Q is -C(R₄)-.

14. A compound according to claim 13 wherein X is -S(O)₂-.

15. A compound according to claim 14 wherein R₉ is hydrogen or methyl.

16. A compound according to claim 2 wherein Q is -N-.

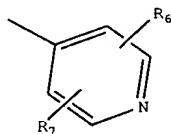
17. A compound according to claim 14 wherein X is a direct link.

18. A compound according to claim 17 wherein R₁ is substituted or unsubstituted aralkyl.

19. A compound according to claim 18 wherein R₉ is hydrogen.

20. A compound according to claim 19 wherein w is 0 or 1.

21. A compound according to claim 1 wherein E is



22. A compound according to claim 21 wherein R₆ and R₇ are independently hydrogen or halogen.

23. A compound according to claim 22 wherein at least one of R₆ and R₇ is hydrogen.

24. A compound according to claim 21 wherein V is -C(R₉)-.

25. A compound according to claim 24 wherein R₉ is hydrogen or methyl.

26. A compound according to claim 2 wherein X is -S(O)₂- or a direct link.

27. A compound according to claim 26 wherein R₁ is unsubstituted aralkyl, substituted aralkyl or alkyl substituted with cycloalkyl in which the cycloalkyl group is substituted with aryl or heteroaryl.

28. A compound according to claim 27 wherein R₂ is hydrogen and R₃ is hydrogen or methyl.

29. A compound according to claim 28 wherein R₃ is methyl.

30. A compound according to claim 29 wherein Q is -N-.

31. A compound according to claim 30 wherein X is a direct link.

32. A compound according to claim 31 wherein R₁ is selected from 2,2-dihalo-2-phenyl-ethyl, 2-(1-phenylcyclopropyl)-ethyl and 2-(1-pyridylcyclopropyl)-ethyl.

33. A compound according to claim 1 selected from the compounds depicted in Figures 1A and 1B.

34. A pharmaceutical composition for treating or decreasing the incidence of a condition in a mammal characterized by

5 abnormal thrombosis, comprising a therapeutically acceptable carrier, and a therapeutically effective amount of compound of claim 1.

10 35. A pharmaceutical composition for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising a therapeutically acceptable carrier, and a therapeutically effective amount of compound of claim 2.

15 36. A pharmaceutical composition for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising a therapeutically acceptable carrier, and a therapeutically effective amount of compound of claim 6.

20 37. A pharmaceutical composition for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising a therapeutically acceptable carrier, and a therapeutically effective amount of compound of claim 15.

25 38. A pharmaceutical composition for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising a therapeutically acceptable carrier, and a therapeutically effective amount of compound of claim 19.

30 39. A pharmaceutical composition for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising a therapeutically acceptable carrier, and a therapeutically effective amount of compound of claim 31.

40. A pharmaceutical composition for treating or decreasing the incidence of a condition in a mammal characterized by

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abnormal thrombosis, comprising a therapeutically acceptable carrier, and a therapeutically effective amount of compound of claim 32.

10 41. A pharmaceutical composition for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising a therapeutically acceptable carrier, and a therapeutically effective amount of compound of claim 33.

15 42. A method for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 1.

20 43. A method for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 2.

25 44. A method for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 6.

30 45. A method for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 15.

46. A method for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 19.

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47. A method for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis,

comprising administering to said mammal a therapeutically effective amount of the compound of claim 31.

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48. A method for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 32.

10 49. A method for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 33.

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